# High density placental mesenchymal stromal cells provide neuronal preservation and improve motor function following in utero treatment of ovine myelomeningocele.

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**Public Summary:**
The goal of this study was to determine if seeding placental derived stem cells at different doses on an extracellular matrix (ECM) patch during fetal repair of spina bifida in a sheep model would result in improved motor function and preserved spinal neurons in a dose dependent manner. METHODS: Spina bifida was surgically created in 33 lambs, and each lamb was repaired with one of the four different placenta stem cell doses on ECM. The four doses were: No cells - ECM only control (n=10), low dose (42K cells/cm2) (n=8), medium dose (167K cells/ cm2) (n=7), or high dose (250-300K cells/ cm2) (n=8). After the lambs were born, their motor function was evaluated using the Sheep Locomotor Rating Scale. A series of cross section slices were then made through the middle of the spina bifida defect in the spinal cord for each lamb. The cross sectional area of the spinal cord in each slice was measured and compared to spinal cord sections take from normal lambs. Large neurons in the spinal cord slices were counted manually and the sum was divided by the cross sectional area of the gray matter in order to calculate the number of neurons per mm2 of gray matter. RESULTS: lambs treated with any dose of placental derived stem cells had a higher median locomotor score (15) than lambs that were treated with only the ECM patch without stem cells (score of 6.5). Cross-sectional areas of spinal cord and gray matter were highest in the medium dose group. Large neuron density was highest in the high dose group, which positively correlated with locomotor score. CONCLUSIONS: Fetal repair of spina bifida with a high dose of placental stem cells on a ECM patch resulted in increased large neuron density in the spinal cord, which strongly correlated with improved motor function.

**Scientific Abstract:**
PURPOSE: The purpose of this study was to determine whether seeding density of placental mesenchymal stromal cells (PMSCs) on extracellular matrix (ECM) during in utero repair of myelomeningocele (MMC) affects motor function and neuronal preservation in the ovine model. METHODS: MMC defects were surgically created in 33 fetuses and repaired following randomization into four treatment groups: ECM only (n=10), PMSC-ECM (42K cells/cm(2)) (n=8), PMSC-ECM (167K cells/cm(2)) (n=7), or PMSC-ECM (250-300K cells/cm(2)) (n=8). Motor function was evaluated using the Sheep Locomotor Rating Scale (SLR). Serial sections of the lumbar spinal cord were analyzed by measuring their cross-sectional areas which were then normalized to normal lambs. Large neurons (LN, diameter 30-70mum) were counted manually and density calculated per mm(2) gray matter. RESULTS: Lambs treated with PMSCs at any density had a higher median SLR score (15 [IQR 13.5-15]) than ECM alone (6.5 [IQR 4-12.75], p=0.036). Cross-sectional areas of spinal cord and gray matter were highest in the PMSC-ECM (167K/cm(2)) group (p=0.002 and 0.006, respectively). LN density was highest in the greatest density PMSC-ECM (250-300K/cm(2)) group (p=0.045) which positively correlated with SLR score (r=0.807, p<0.0001). CONCLUSIONS: Fetal repair of myelomeningocele with high density PMSC-ECM resulted in increased large neuron density, which strongly correlated with improved motor function. TYPE OF STUDY: Basic science. LEVEL OF EVIDENCE: N/A.